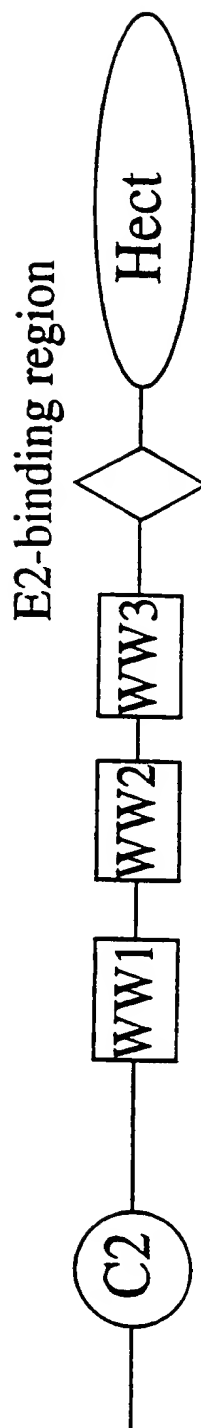


# Rat Nedd4

Figure1



[illegible]

Figure 2: Clone 7.7 is the homolog of human clone KIAA0313

- Clone 7.7 exhibits 75% identity and 95% similarity of human clone KIAA0313.

**2/34**

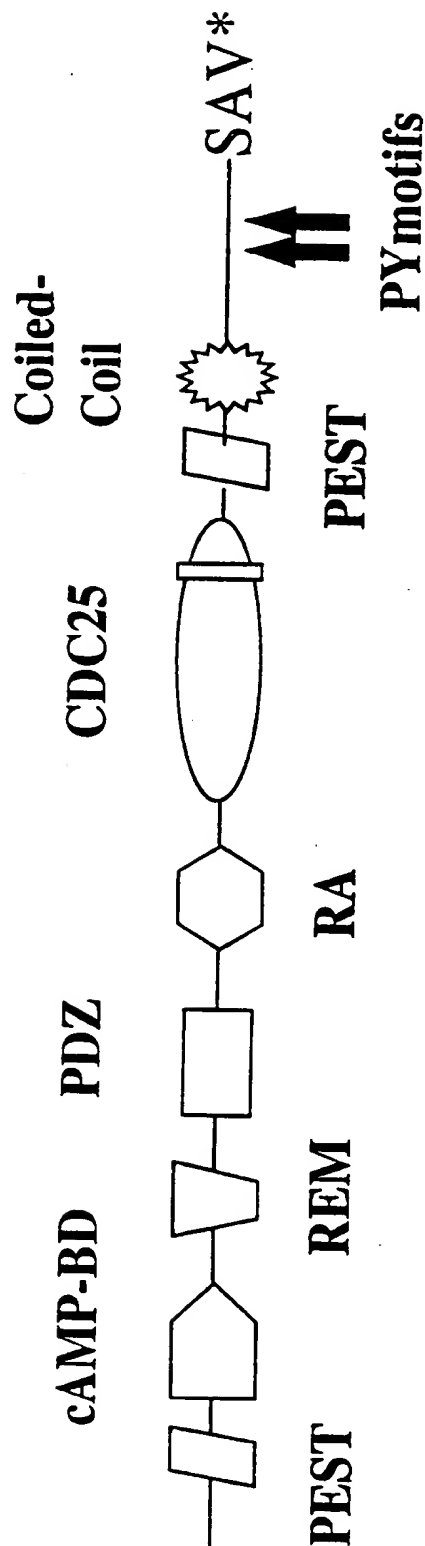
Clone7.7  
KIAA0313

GKKDVSAEAESSSMVPVTTTEAKPVMPPAHIAVTPTTKGLIARKEGRYREPPPTPGYV  
GKKDVSIEAESSSLTSVTTEETKPVMPPAHIAVASSTTKGLIARKEGRYREPPPTPGYI  
\*\*\*\*\* : .. \*\*\*\*\* : \*\*\*\*\* : \*\*\*\*\* :

Clone7.7  
KIAA0313

Clone7.7  
KIAA0313

Figure 3A Schematic Diagram of GRF4



4618 b.p.

1/1 31/11  
 atg aaa cca cta gca atc cca gct aac cat gga gtt atg ggc cag cag gag aaa cac tca  
 M K P L A I P A N H G V M G Q Q E K H S  
 61/21 91/31  
 ctt cct gca gat ttc aca aaa ctg cat ctt act gac agt ctc cac cca cag gtg acc cac  
 L P A D F T K L H L T D S L H P Q V T H  
 121/41 151/51  
 gtt tct tct agc cat tca gga tgt agt atc act agt gat tct ggg agc agc agt ctt tct  
 V S S S H S G C S I T S D S G S S S L S  
 181/61 211/71  
 gat atc tac cag gcc aca gaa agc gag gct ggt gat atg gac ctg agt ggg ttg cca gaa  
 D I Y Q A T E S E A G D M D L S G L P E  
 241/81 271/91  
 aca gca gtg gat tcc gaa gac gac gac gat gaa gaa gac att gag aga gca tca gat cct  
 T A V D S E D D D D E E D I E R A S D P  
 301/101 331/111  
 ctg atg agc agg gac att gtg aga gac tgc cta gag aag gac cca att gac cgg aca gat  
 L M S R D I V R D C L E K D P I D R T D  
 361/121 391/131  
 gat gac att gaa caa ctc ttg gaa ttt atg cac cag ttg cct gct ttt gcc aat atg aca  
 D D I E Q L L E F M H Q L P A F A N M T  
 421/141 451/151  
 atg tca gtg agg cga gaa ctc tgt gct gtg atg gtg ttc gca gtg gtg gaa aga gca ggg  
 M S V R R E L C A V M V F A V V E R A G  
 481/161 511/171  
 acc ata gtg tta aat gat ggt gaa gag ctg gac tcc tgg tca gtg att ctc aat gga tct  
 T I V L N D G E E L D S W S V I L N G S  
 541/181 571/191  
 gtg gaa gtg act tat cca gat gga aaa gca gaa ata ctg tgc atg gga aat agt ttt ggt  
 V E V T Y P D G K A E I L C M G N S F G  
 601/201 631/211  
 gtc tct cct acc atg gac aaa gaa tac atg aaa gga gtg atg aga aca aag gtg gat gac  
 V S P T M D K E Y M K G V M R T K V D D  
 661/221 691/231  
 tgc cag ttt gtc tgc ata gcc cag caa gat tac tgc cgt att ctc aat caa gta gaa aag  
 C Q F V C I A Q Q D Y C R I L N O V E K  
 721/241 751/251  
 aac atg caa aaa gtt gaa gag gaa gga gag att gtt atg gtg aaa gaa cac cga gaa ctt  
 N M Q K V E E E G E I V M V K E H R E L  
 781/261 811/271  
 gat cga act gga aca aga aag gga cac att gtc atc aag ggt acc tca gaa agg tta aca  
 D R T G T R K G H I V I K G T S E R L T  
 841/281 871/291  
 atg cat ttg gtg gaa gag cat tca gta gta gat cca aca ttc ata gaa gac ttt ctg ttg  
 M H L V E E H S V V D P T F I E D F L L  
 901/301 931/311  
 acc tat agg act ttt ctt tct agc cca atg gaa gtg ggc aaa aag tta ttg gag tgg ttt  
 T Y R T F L S S P M E V G K K L L E W F  
 961/321 991/331  
 aat gac cag agc ctc agg gat aag gtt aca cgg gta gta tta ttg tgg gta aat aat cac  
 N D P S L R D K V T R V V L L W V N N H  
 1021/341 1051/351  
 ttc aat gac ttt gaa gga gat cct gca atg act cga ttt tta gaa gaa ttt gaa aac aat  
 F N D F E G D P A M T R F L E E F E N N

cNMP-BD

REM

(continued next page)

Figure 3B

4/34

1081/361

1111/371

ctg gaa aga gag aaa atg ggt gga cac cta agg ctg ttg aat atc gcg tgt gct gct aaa  
L E R E K M G G H L R L L N I A C A A K

1141/381

1171/391

gca aaa aga aga ttg atg acg tta aca aaa cca tcc cga gaa gct cct ttg cct ttt atc  
A K R R L M T L T K P S R E A P L P F I

1201/401

1231/411

tta ctt gga ggc tct gag aag gga ttt gga atc ttt gtt gac agt gta gat tca ggt agc  
L L G G S E K G F G I F V D S V D S G S

1261/421

1291/431

aaa gca act gaa gca ggc ttg aaa cgg ggg gat cag ata tta gaa gta aat ggc caa aac  
K A T E A G L K R G D O I L E V N G Q N

1321/441

1351/451

ttt gaa aac att cag ctg tca aaa gct atg gaa att ctt aga aat aac aca cat tta tct  
F E N I O L S K A M E I L R N N T H L S

1381/461

1411/471

atc act gtg aaa acc aat tta ttt gta ttt aaa gaa ctt cta aca aga ttg tca gaa gag  
I T V K T N L F V F K E L L T R L S E E

1441/481

1471/491

aaa aga aat ggt gcc ccc cac ctt cct aaa att ggt gac att aaa aag gcc agt cgc tac  
K R N G A P H L P K I G D I K K A S R Y

1501/501

1531/511

tcc att cca gat ctt gct gta gat gta gaa cag gtg ata gga ctt gaa aaa gtg aac aaa  
S I P D L A V D V E Q V I G L E K V N K

1561/521

1591/531

aaa agt aaa gcc aac act gtg gga gga agg aac aag ctg aaa aag ata ctc gac aag act  
K S K A N T V G G R N K L K K I L D K T

1621/541

1651/551

cgg atc agt atc ttg cca cag aaa cca tac aat gat att ggg att ggt cag tct caa gat  
R I S I L P Q K P Y N D I G I G Q S Q D

1681/561

1711/571

gac agc ata gta gga tta agg cag aca aag cac atc cca act gca ttg cct gtc agt gga  
D S I V G L R Q T K H I P T A L P V S G

1741/581

1771/591

acc tta tca tcc agt aat cct gat tta ttg cag tca cat cat cgc att tta gac ttc agt  
T L S S S N P D L L Q S H H R I L D F S

1801/601

1831/611

gct act cct gac ttg cca gat caa gtg cta agg gtt ttt aag gct gat cag caa agc cgc  
A T P D L P D Q V L R V F K A D O Q S R

1861/621

1891/631

tac atc atg atc agt aag gac act aca gca aag gaa gtg gtc att cag gct atc agg gag  
Y I M I S K D T T A K E V V I O A I R E

1921/641

1951/651

ttt gct gtt act gcc acc ccg gat caa tat tca cta tgt gag gtc tct gtc aca cct gag  
F A V T A T P D O Y S L C E V S V T P E

1981/661

2011/671

gga gta atc aaa caa aga aga ctt cca gat cag ctt tcc aaa ctt gca gac aga ata caa  
G V I K O R R L P D O L S K L A D R I O

2041/681

2071/691

ctg agt gga agg tat tat ctg aaa aac aac atg gaa aca gaa act ctt tgt tca gat gaa  
L S G R Y Y L K N N M E T E T L C S D E

2101/701

2131/711

gat gct cag gag ttg ttg aga gag agt caa att tcc ctc ctt cag ctc agc act gtg gaa  
D A Q E L L R E S Q I S L L O L S T V E

2161/721

2191/731

gtt gca aca cag ctc tct atg cga aat ttt gaa ctc ttt cgc aac att gaa cct act gaa  
V A T O L S M R N F E L F R N I E P T E

PDZ

RA

(continued next page)

5/34

### Continuation of the CDC25 domain

**SUBSTITUTE SHEET (RULE 26)**

3361/1121 3391/1131  
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 P Q S S P R K G Y T L A P S G T V D N F  
 3421/1141 3451/1151  
 tca gat tct ggt cac agt gaa att tct tca cga tcc agt att gtt agc aat tct tct tt  
 S D S G H S E I S S R S S I V S N S S F  
 3481/1161 3511/1171  
 gac tca gtg cca gtc tca ctg cac gat gag agg cgc cag agg cat tct gtc agc atc gtg  
 D S V P V S L H D E R R Q R H S V S I V  
 3541/1181 3571/1191  
 gaa aca aac cta ggg atg ggc agg atg gag agg cgg acc atg att gaa cct gat cag tat  
 E T N L G M G R M E R R T M I E P D Q Y  
 3601/1201 3631/1211  
 agc ttg ggg tcc tat gca cca atg tcc gag ggc cga ggc tta tat gct aca gct aca gta  
 S L G S Y A P M S E G R G L Y A T A T V  
 3661/1221 3691/1231  
 att tct tct cca agc aca gag gaa ctt tcc cag gat cag ggg gat cgc gcg tca ctt gat  
 I S S P S T E E L S Q D Q G D R A S L D  
 3721/1241 3751/1251  
 gct gct gac agt ggc cgt ggg agc tgg acg tca tgc tca agt ggc tcc cat gat aat ata  
 A A D S G R G S W T S C S S G S H D N I  
 3781/1261 3811/1271  
 cag acg atc cag cac cag aga agc tgg gag act ctt cca ttc ggg cat act cac tt gat  
 Q T I Q H Q R S W E T L P F G H T H F D  
 3841/1281 3871/1291  
 tat tca ggg gat cct gca ggt tta tgg gca tca agc agc cat atg gac caa att atg tt  
 Y S G D P A G L W A S S S H M D Q I M F  
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 S D H S T K Y N R Q N Q S R E S L E Q A  
 3961/1321 3991/1331  
 cag tcc cga gca agc tgg gcg tct tcc aca ggt tac tgg gga gaa gac tca gaa ggt gac  
 Q S R A S W A S S T G Y W G E D S E G D  
 4021/1341 4051/1351  
 aca ggc aca ata aag cgg agg ggt gga aag gat gtt tcc att gaa gcc gaa agc agt agc  
 T G T I K R R G G K D V S I E A E S S S  
 4081/1361 4111/1371  
 cta acg tct gtg act acg gaa gaa acc aag cct gtc ccc atg cct gcc cac ata gct gtg  
 L T S V T T E E T K P V P M P A H I A V  
 4141/1381 4171/1391  
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 A S S T T K G L I A R K E G R Y R E P P  
 4201/1401 4231/1411  
 ccc acc cct ccc ggc tac att gga att ccc att act gac tt cca gaa ggg cac tcc cat  
 P T P P G Y I G I P I T D F P E G H S H  
 4261/1421 4291/1431  
 cca gcc agg aaa ccg ccg gac tac aac gtg gcc ctt cag aga tgc cgg atg gtc gca cga  
 P A R K P P D Y N V A L Q R S R M V A R  
 4321/1441 4351/1451  
 tcc tcc gac aca gct ggg cct tca tcc gta cag cag cca cat ggg cat ccc acc agc agc  
 S S D T A G P S S V Q Q P H G H P T S S  
 4381/1461 4411/1471  
 agg cct gtg aac aaa cct cag tgg cat aaa ccg aac gag tct gac ccg cgc ctc gcc cct  
 R P V N K P Q W H K P N E S D P R L A P

PY motifs

(continued next page)

4441/1481

4471/1491

tat cag tcc caa ggg ttt tcc acc gag gag gat gaa gat gaa caa gtt tct gct gtt tga  
Y Q S Q G F S T E E D E D E Q V S A V \*

4501/1501

4531/1511

### PDZ binding motif

ggc aca gac ttt tct gga agc aga ggc agc cac ctg aaa gga gag cac aag aag acg tcc  
G T D F S G S R A S H L K G E H K K T S

4561/1521

4591/1531

\* A L E P W N S H S E D G G P V C L L



# CDC25 Domain

hGRF4 SQISLLQLSTVEVATQLSMRNFELFRNIEPTHEYIDDLF---KLRSKTSCANLKRFEVIN  
dGRF4 SNVHFLHLNAYELAIQLTLQDFANFRQIESTEYVDELF---ELRSRYGVPMLSKFAELVN  
hEpac SAEGLDLVSADLAGQLTDHDSLFNSIHQVELIHVYLGPOHLRDVT-TANLERFMRRFN  
mRasGRF2 KAECFETLSAMELAEQITLLDHIVFRSIPYEEFLGQGW--MKLDKNERTPYIMKTSQHFN  
dSOS DEITLLTLHPLRLARQLTLLEFEMYKNVKPSELVGSPT--KKDKEVKSPNLLKIMKHTT  
hRasGRP VSLFLDHLEPEELSEHLTYLEFKSFRRISFSDYQNYLVN----SCVKENPTMERSIALCN  
: : . : : : : : : : : : : : .

hGRF4 QETFWVASEILRETNQLKRMKIIKHFIKIALHCRECKNFNSHFAIISGLNLAPVARLRTT  
dGRF4 REMFWVSEICAENIVRRMKIVKQFIKIAHCKEKNFNSHFAIVSGLGHGAVSRLRQT  
hEpac ELQYVATELCLCPVGPRAQLLRKFIKLAHLKEQKNLNSFFAVMFGLSNSAISRLAHT  
mRasGRF2 EMSNLVASQIMNYADISSRPNAIEKWVAVADICRCLHNYNGVLEITSALNRSPIYRLKKT  
dSOS NVTRWIEKSITEAENYEERLAIHQRAIEVHHVHLELNNFNGILSIVAAMGTASVYRLRWT  
hRasGRP GISQWVQLMVLRSPTPQLRAEVFIKFIQVAQKLHQLQNFNTLMAVIGGLCHSSISRLKET  
: : \* : : : : \* \* : : : : \* \*

hGRF4 WEKLPNKYEKLFQDLQDLFDPSRNMAYRNVLNSQNL-QPPIIPLFPVIKKDLTFLHEGN  
dGRF4 WEKLPISKYQRLFNDLQDLMDPSRNMASKYRQLVSAELLAQHPIIPFPYIVKKDLTFIHLGN  
hEpac WERLPHKVRKLYSALERLLDPSWNHRVYR-LALAKLS--PPVIPFMPLLLKDMTFIHEGN  
mRasGRF2 WAKVSKQTKALMDKLQKTVSSEGRFKNLR-ETLKNCN--PPAVPYLGMYLTDLAFIEEGT  
dSOS FQGLPERYRKFLKEECRELSDDHLKKYQER--L-RSIN--PPCVPPFGRYLTNHLHEEGN  
hRasGRP SSHVPHEINKVLGEMTELLSSSRNYDNYR-RAYGECT--DFKIPILGVHLKDLISLYEAM  
: . . . . \* . : \* : : : .

hGRF4 DSKVDG--LVNFEKLRMIAKEIRHVGRMASVNMDPALMFRTRKKK---WRSLSLSQGS  
dGRF4 DTRVDG--LINFELRLMLAKEVRLLTHMCSSPYDLLSILELKGQSPSNALFSLNQMSASQ  
hEpac HTLVEN--LINFEMRMARAARMLHHCRRSHNPVPLSPLRSRVSHLHEDSQVARISTCSE  
mRasGRF2 PNFTEEG-LVNFSKMRMISHIIREIROQFQOTAYRIDQOP-----  
dSOS PDLLANTELINFSKRRKVAEIIIGEIQQYQNPYCLNEES-----  
hRasGRP PDYLEDG-KVNVRHLLALYNHISELVQLQEVAPPLEANKDL-----  
: \* . : : : .

hGRF4 TNATVLDVAQTGG----HKKRVRRSSFLNAKKLYEDAQMARKVKQYLSNLELEMDDEESIQ  
dGRF4 SNAAAGTVIAANAGQATIKRRKKSTAAPNPKKMFEEAQMVRRVKAYLSNLKILSDEDLH  
hEpac -----QSLSTRSPASTWAYVQQLKVIDNQRELS  
mRasGRF2 -----KVIQYLLDKALVIDEDSLY  
dSOS -----TIROFFEQLDPFNGLSKQMSDYLY  
hRasGRP -----VHLLTSLDLYYTEDEIY  
: : .

hGRF4 TLSLQCEPATNT  
dGRF4 KFSLECEPAHGS  
hEpac RLSRELEP----  
mRasGRF2 ELSLKIEPRLPA  
dSOS NESLRIEPRGCK  
hRasGRP ELSYAREPRNHR  
\* \*\*

Figure 4

FIG. 5

# Figure 5: GRF4-REM domain

|                 |  |
|-----------------|--|
| CDC25           | -IRGGTKEALIEHLT-SHELVDAAFNVMTLITFRSILT-TREFFYALIYRY- |
| Sos_mouse_      | -IKGGTVVVKLIERLT-YHMYADPNF-VRTFLTYRSFCK-PQELNLLIERFE |
| RasGEF_aimless_ | VVKFASLNKLVVEHLT-HDSKHDLOFLKTFMLTYQSFT-PEKLSKLQORY-  |
| GRF2_mouse_     | -IRYASVEALLERLT-DLRFSLIDFLNTFLHTYRIFTT-ATVVLAKLSDIY- |
| GRF4            | -IKG-TSERLTMLVEEHSVVDPTFIEDFLTYRTFLSSPMEVGKLLLEWFN   |
|                 | :: : * : * . . . . . * :                             |

FIG. 6A

Figure 6A:

# Overall structure comparison between GRF4 and other known mammalian

## RasGEF/RasGRF

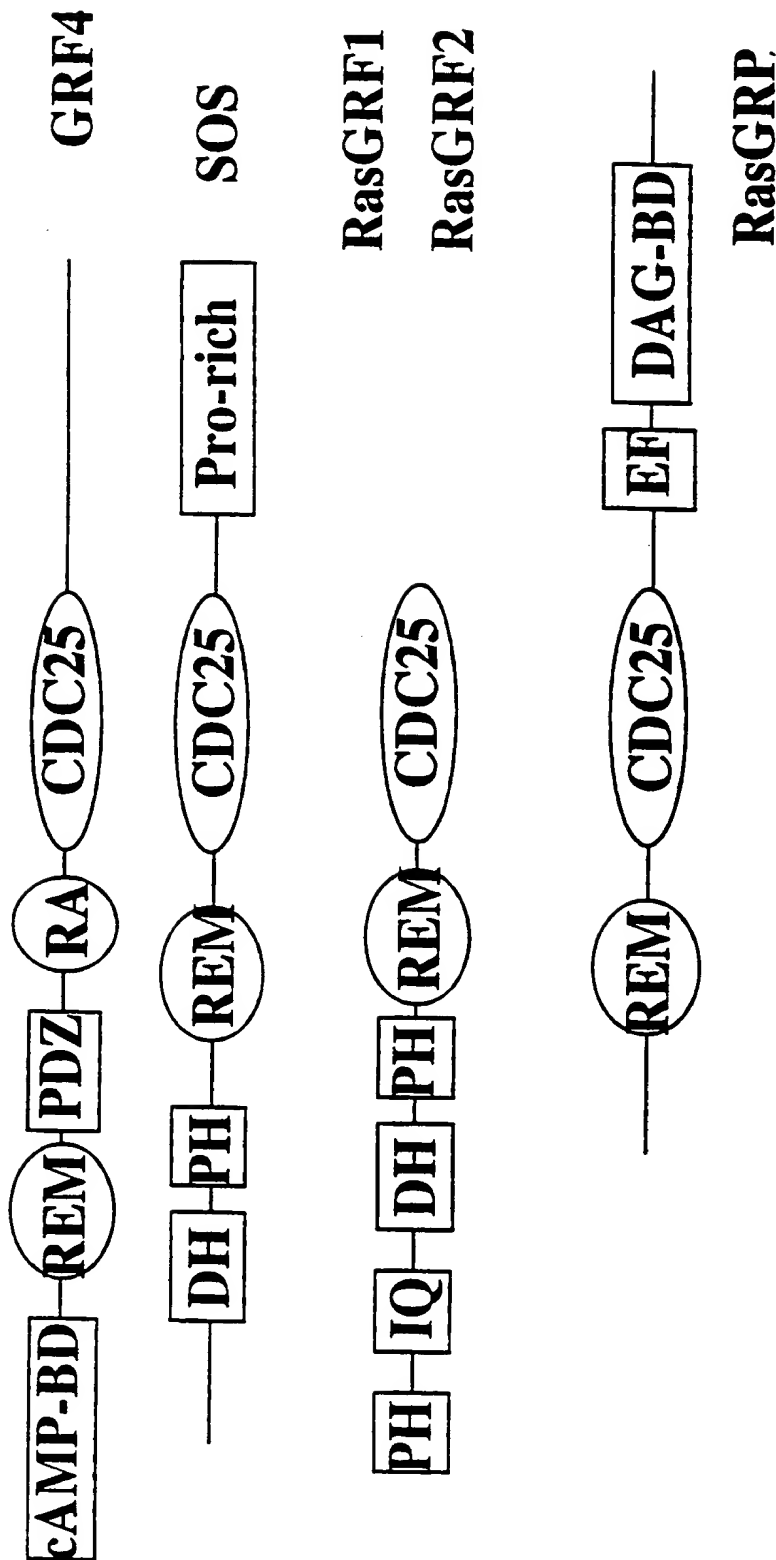
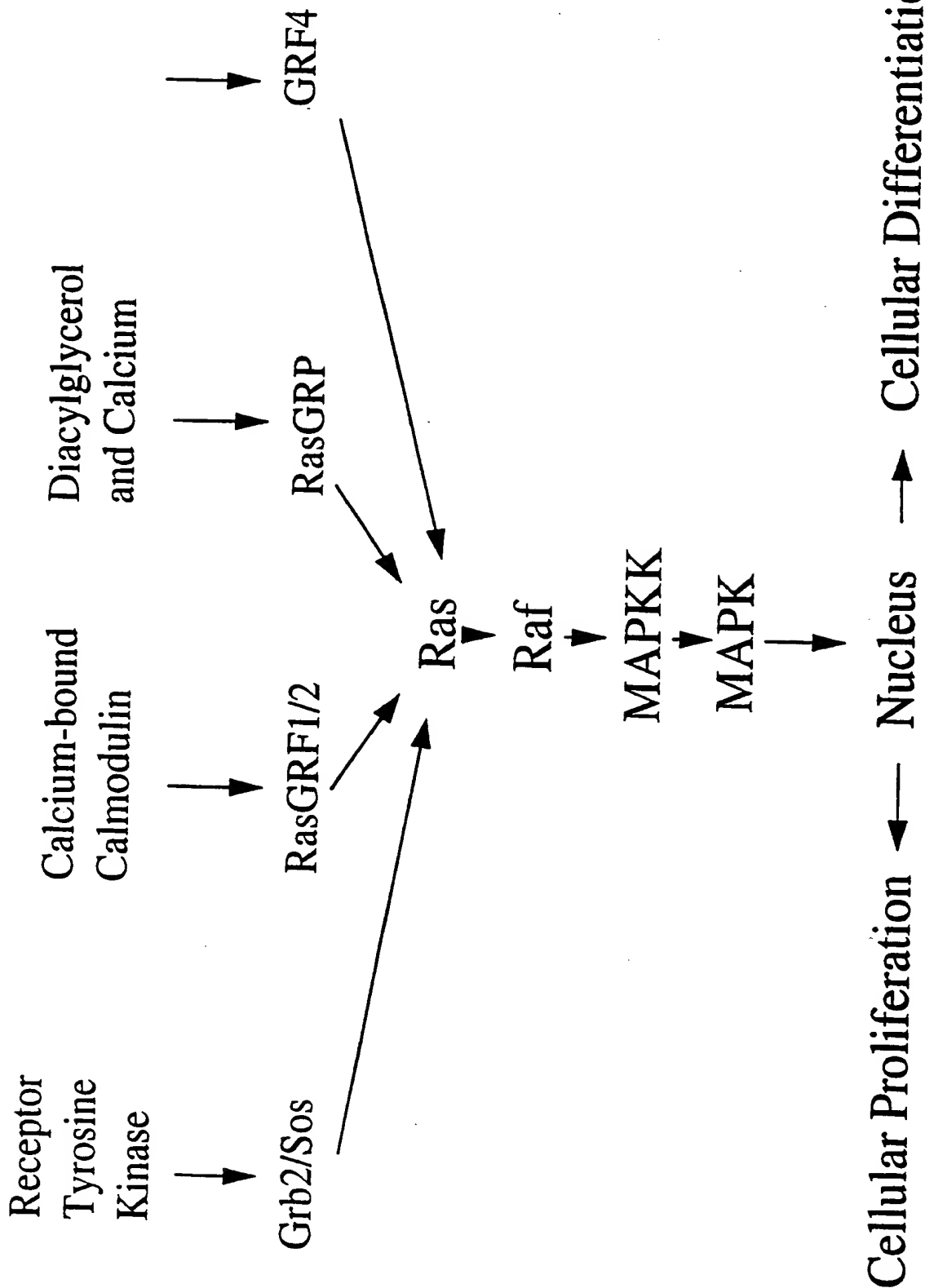


FIG. 6B

# Ras Signaling pathway



12/34

100220" 9281660

Figure 7

# PDZ domain

|            |  |
|------------|--|
| hGRF4      | LTKPSREAPLPFILLGSEK-----GFGIFVDSVDSGSKATEAG-LKRGDQIL       |
| dGRF4      | LTRSSRDEPLNFRIVGGYELRGVAIATGNAAVGIYISHVEPGSKAQDVG-LKRGDQIH |
| hPTP-BAS-1 | NLKKDAKYGLGFQIIGGEKMGRL-----DLGIFISSVAPGGPADLDGCLKPGDRLI   |
| hPSD-95    | IVIHRGSTGLGFNIVGGEDG-----EGIFISFILAGGPADLSGELRKGDQIL       |
| rLin-7-C   | VELPKTEEGLGFNIMGKEQ-----NSPIYISRIIPGGIADRHGGLKRGDQLL       |
| hDGL       | VKVQKGSEPLGISIVSGEK-----GIYVSKVTVGSIAHQAG-LEYGDQLL         |
|            | . * : : : * . * : : : * . * : : : *                        |
| hGRF4      | EVNGQNFENIQLSKAMEILR                                       |
| dGRF4      | EVNGQSLDHVTSKRALEILT                                       |
| hPTP-BAS-1 | SVNSVSLEGVSHHAAIEILQ                                       |
| hPSD-95    | SVNGVDLRNASHEQAAIALK                                       |
| rLin-7-C   | SVNGVSVEGEHHEKAVELLK                                       |
| hDGL       | EFNGINLRSATEQQARLIIG                                       |
|            | ..* . . * :  |

13/34

[illegible]

### Figure 8

# cNMP-BD

hGRF4  
dGRF4  
hEPAC  
PRKAR1B  
hPKGII  
m-EAG

hGRF4  
dGRF4  
hEPAC  
PRKAR1B  
hPKGII  
m-EAG

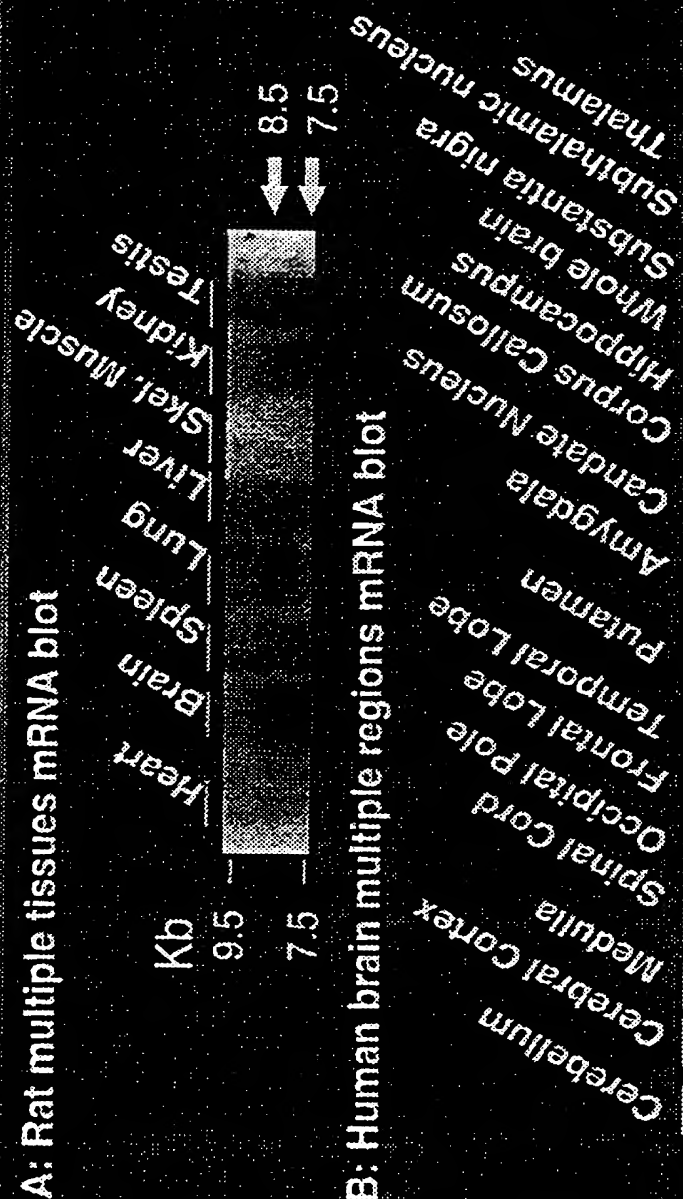
15/34

T00240" 922T660

Figure 10

## Tissue Distribution of GRF4

A: Rat multiple tissues mRNA blot

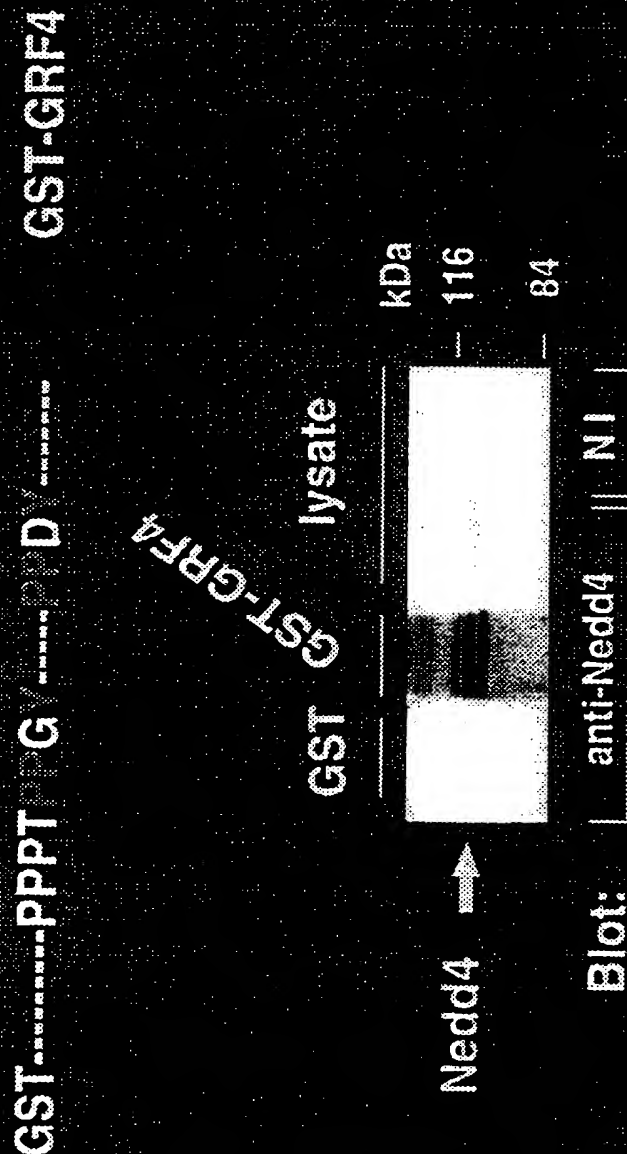




100220" 928TF660

Figure 11

GST-fusion protein of the C-terminal last 150 aa of  
 GRF4 containing two PY motifs pulls down  
 endogenous Nedd4 in Hek 293T cells



100220" 928TF660

Figure 12

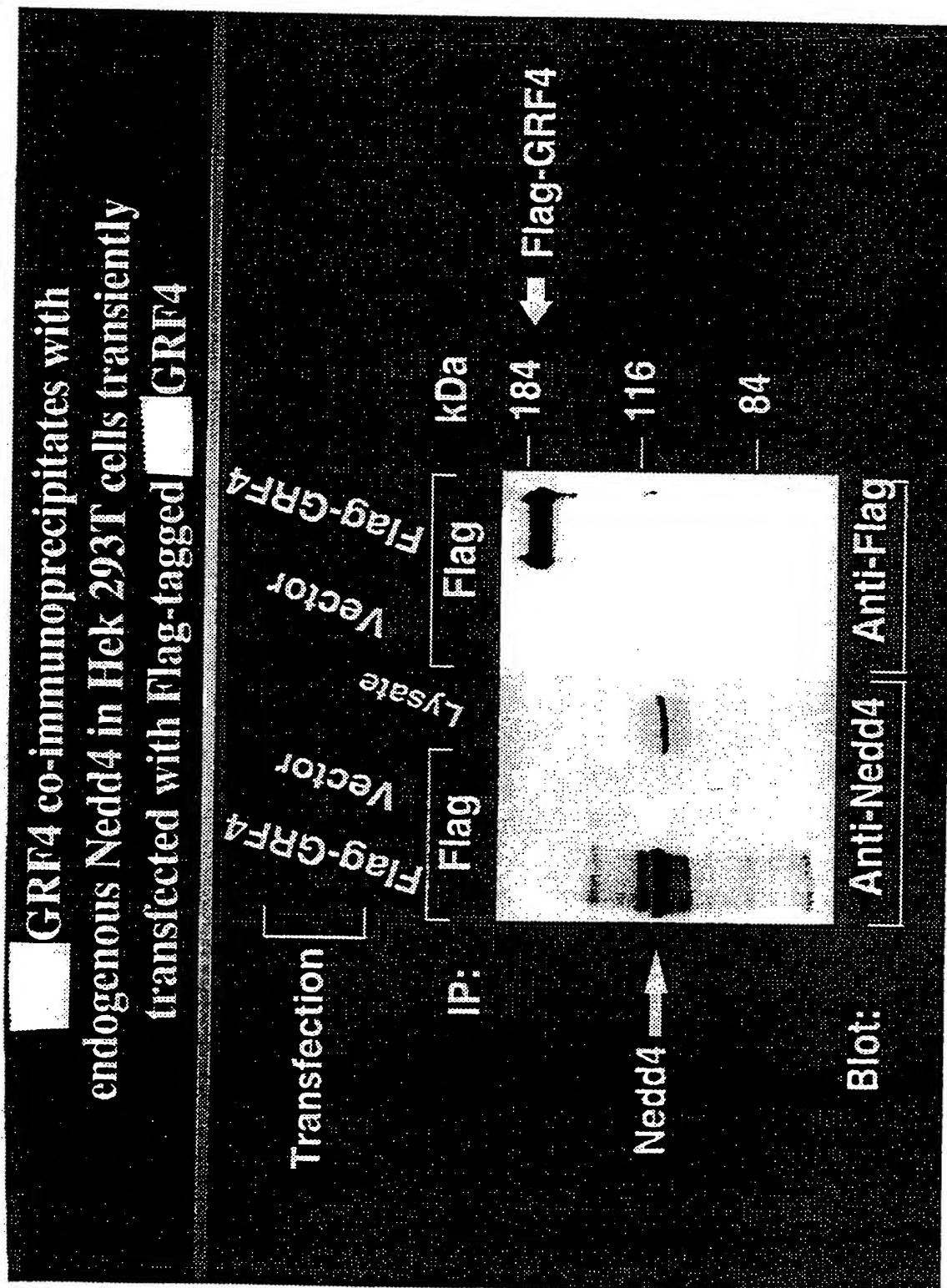


Fig.13

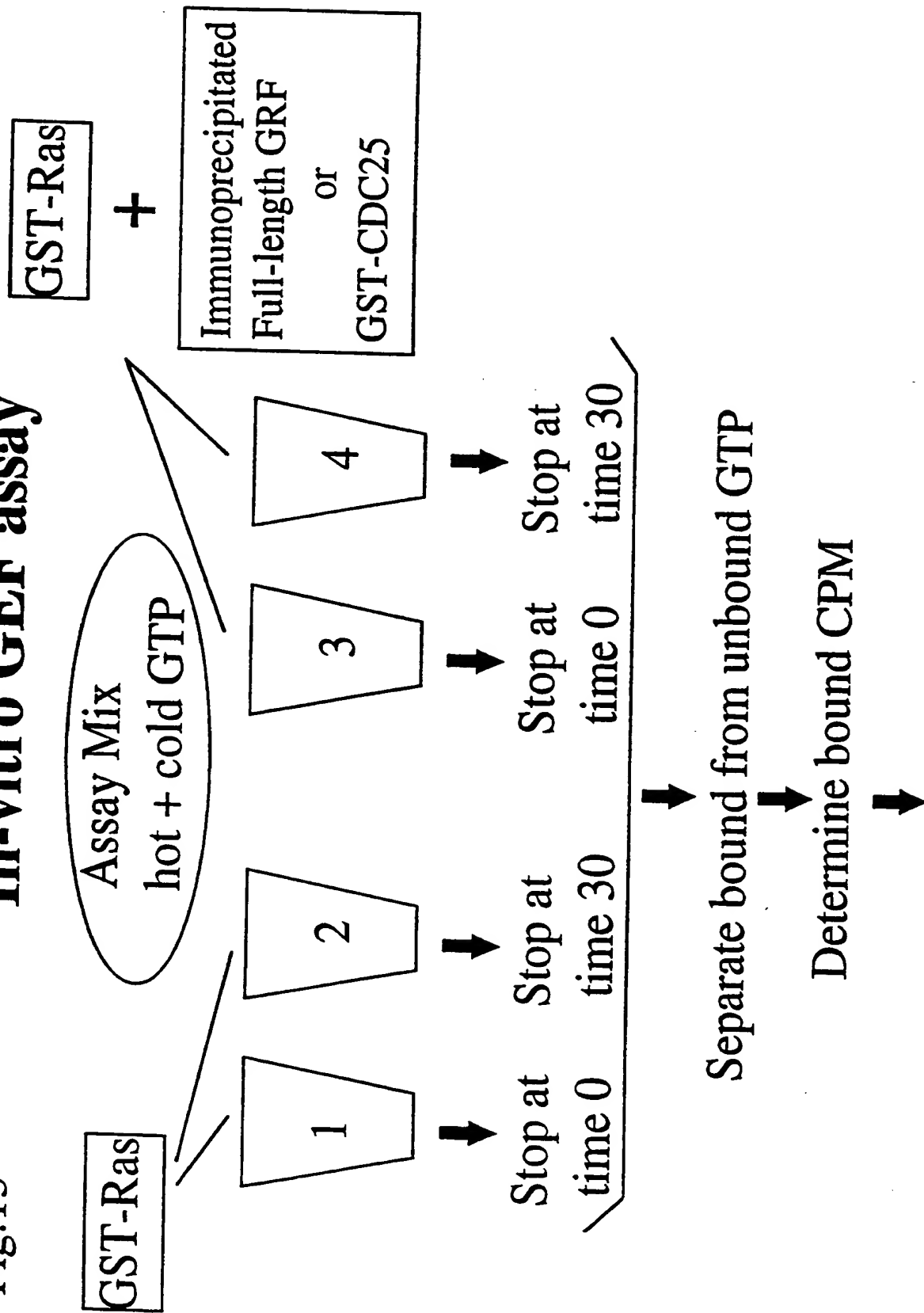
**In-vitro GEF assay**

FIG. 14

Fig.14 GRF4 is active on Ras : in-vitro GEF  
assay using immunoprecipitated full-length  
GRF4

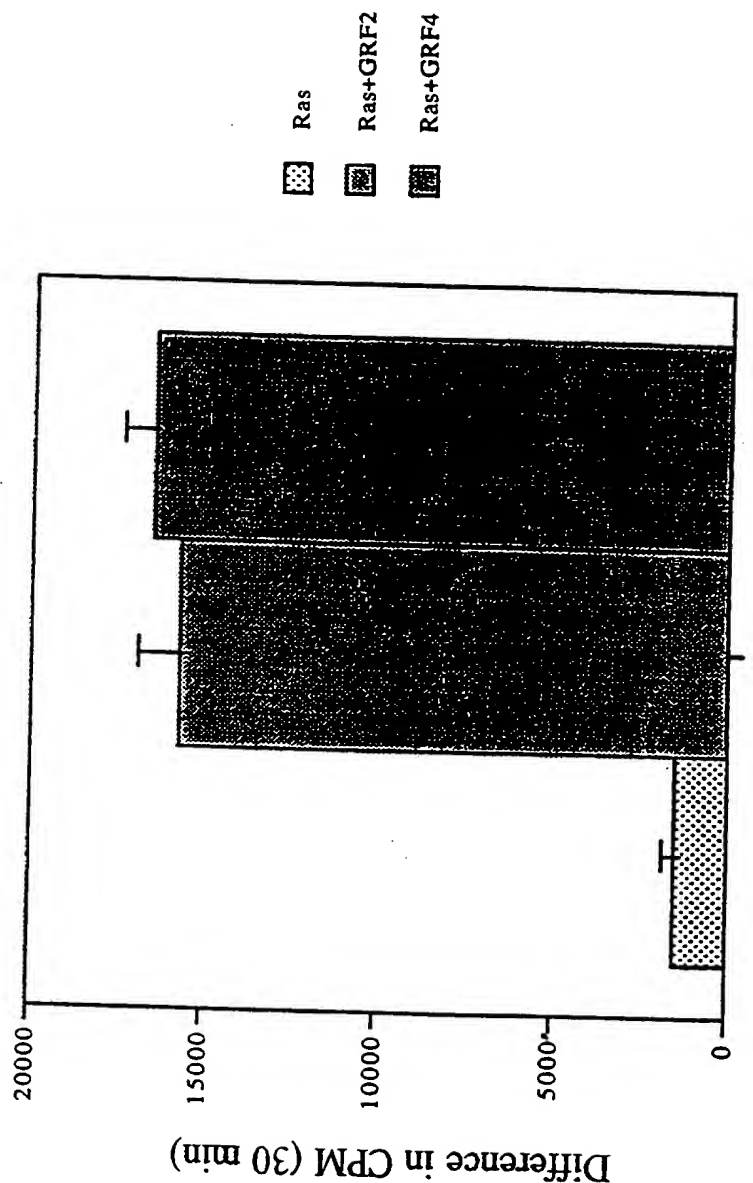


FIG. 15

Figure 15

GRF4 forms stable complex with Ras in-vitro:  
it binds preferentially to nucleotide-free and  
GTP-bound Ras

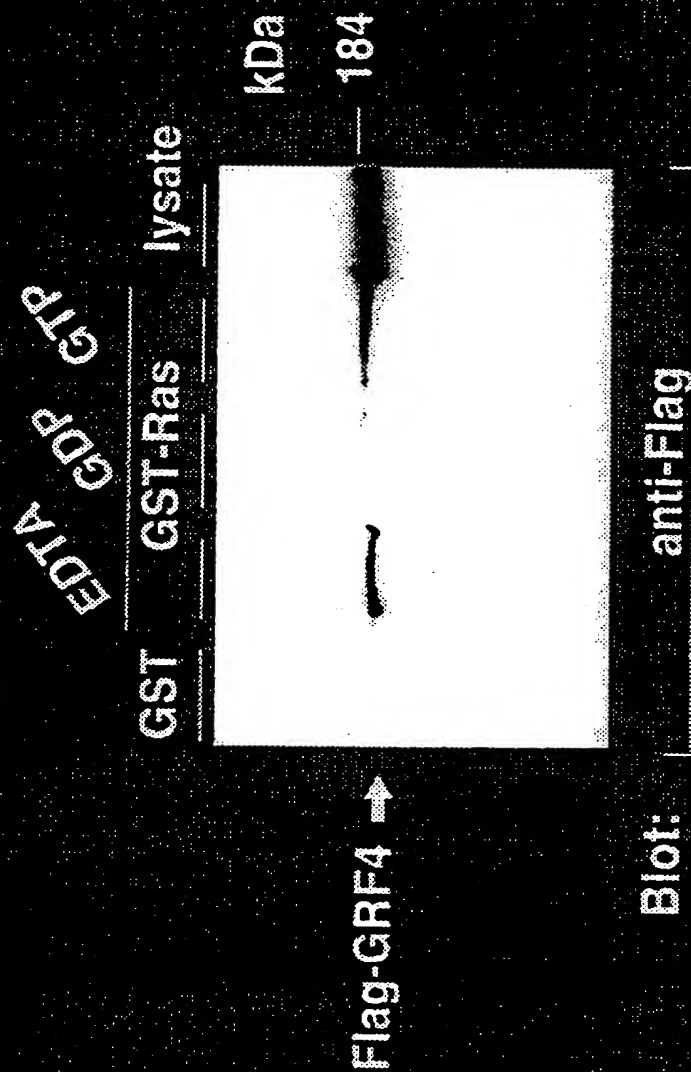


FIG. 16

Figure 16

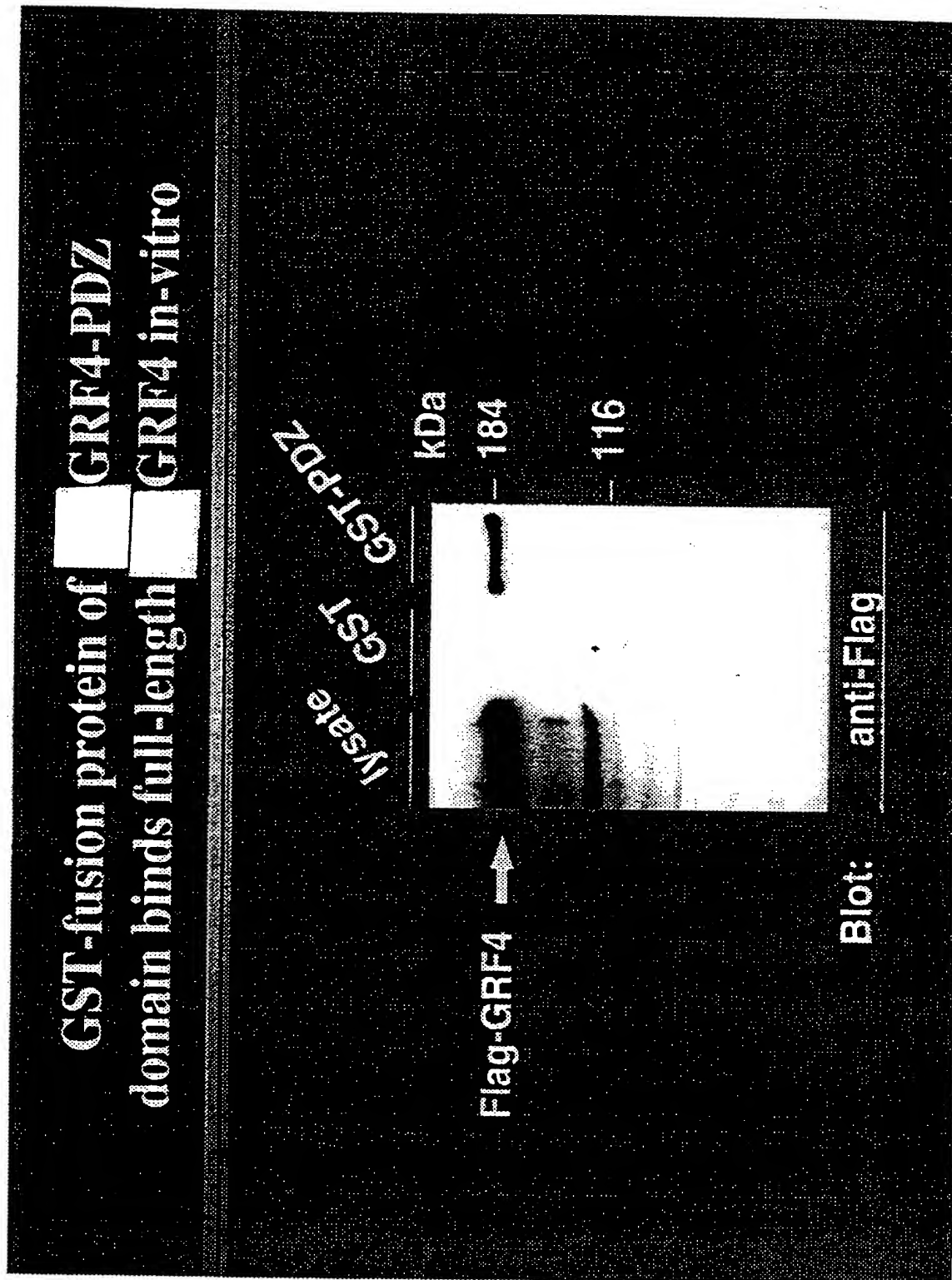
Transformation Assay: GRF4 induces foci formation in Rat2 fibroblasts

Empty Vector GRF4 RasV12



FIG. 20

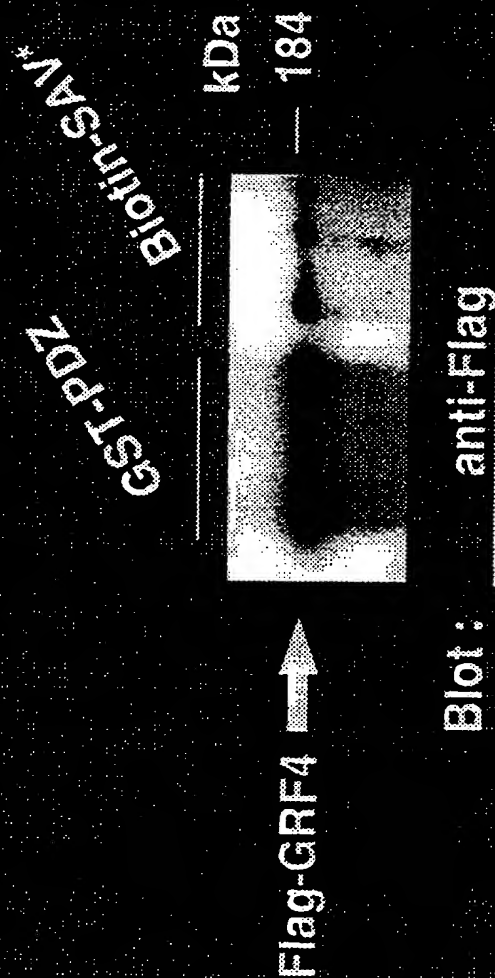
Figure 17



T00220" 928T660

Figure 18

Biotinylated peptide of the last 15 aa sequence of  
 [ ] GRF4 containing the [ ] PDZ-binding  
 motif (SAV\*) binds full-length [ ] GRF4 in-vitro





6568 bp

/translation="MKPLAIPANHGVMGQEQEKHSLPADFTKLHLTDSLHPQVTHVSSS  
 HSGCSITSDSGSSSLSDIYQATESEAGDMDLSGLPETA VDSEDDDDDEEDIERASDPLM  
 SRDIVRDCLEKDPIDRTDDDDIEQLLEFMHQLPAFANMTMSVRRELCAVMVFAVVERAG  
 TIVLNDGEELDSWSVILNGSVEVTPDGKAEILCMGNSFGVSPTMDKEYMKGMVMTKV  
 DDCQFVCIAQQDYCRILNQVEKNMQKVEEEGEIVMVKEHRELDRTGTRKGHIVIKGTS  
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 AVASSTTKGLIARKEGRYREPPPTPPGYIGIPITDFEGHSHPARKPPDYNVALQRSR  
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63. .4562

BASE COUNT 1974 a 1400 c 1463 g 1731 t  
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 181 acgtttcttc tagccattca ggatgtagta tcaactagta ttctgggagc agcagttctt  
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 301 aaacagcagt ggattccgaa gacgacgacg atgaagaaga cattgagaga gcatcagatc  
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 541 ggaccatagt gttaatgat ggtgaagagc tggactcctg gtcagtgtt ctcaatggat  
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(continued next page)

26/34

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4681 cctgccttaa aagcagcatg gggctcttc tccctctctt ccttccctt ttgcatgtga  
4741 aatactgtga agaaattgcc ctggcacttt tcagactttg ttgcttga aa tgcacagtgc  
4801 agcaatcttc gagtccccc tttgtgtgcc tggcacatca cacagtatca ttccaaattc  
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5401 cacatggcca ggggagggaa ctaggacct tgtgtctgt ctgagcctta tggaggcagg  
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6001 attaaattca gctgaatata ttgatcagta gataaacgta aatagcttca aattttaaaa  
6061 gtggaattgc agtgttttt cactgtatca aacaatgtca gtgctttatt taataattct  
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801 b.p.

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 L K G T K A G A P P R W R P L N W I  
 R E Q K L E L H R G G G R S R T S G S

61/21 91/31  
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 P R A A G I Q A V G R M S P L R Q R A A  
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121/41 151/51  
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 S M V P V T T E E A K P V P M P A H I A  
 A W C P L Q R K P N L S L C L P T L  
 H G A R D Y R G S Q T C P Y A C P H S C

181/61 211/71  
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 V T P S T T K G L I A R K E G R Y R E P  
 R R A L P R D S S H G R K A G T G S R  
 D A E H Y Q G T H R T E G R Q V P G A A

241/81 271/91  
 CCT CCC ACA CCT CCA GGC TAC GTG GGC ATC CCC ATT GCC GAT TTC CCA GAA GGG CCT TGC  
 P P T P P G Y V G I P I A D F P E G P C  
 L P H L Q A T W A S P L P I S Q K G L A  
 S H T S R L R G H P H C R F P R R A L P

301/101 331/111  
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 H P A R K P P D Y N V A L Q R S R M V A  
 T R P G S P R I T T W P C S G P A W W H  
 P G Q E A P G L Q R G P A A V P H G G T

361/121 391/131  
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 A H G P G T G P D A A C S R S Q P A G

421/141 451/151  
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 A A S H S G T S P A T Q T H A S R P S S  
 Q Q A T V A Q A Q R R R P T P R A L P A

481/161 511/171  
 CCG CAG GCT TCG CAG GAG CCG AGG AGG ACG AAG ATG AAC AAG TGT CTG CTG TTT GAG GCG  
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 R G L R R S G G G R R T S V C C L R R  
 A G F A G A E E D E D E Q V S A V G A

541/181 571/191  
 CAG GCT CCT TGA TCC ACA GTG AGC CAC CCA AAG GAG AGC ACA AGA AGA CGT CCC AAG CCT  
 Q A P S T V S H P K E S T R R R P K P  
 R L L D P Q A T Q R R A Q E D V P S L  
 G S L I H S E P P K G E H K K T S Q A L

601/201 631/211  
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 W S L G T H I G W W T S L P P S L P  
 G A L A R T S E D G G P V C L L P C L K  
 E P W H A H L R M V D Q F A S F P A L K

661/221 691/231  
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 Q H G A S S P L L P F P F A C E I L R

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721/241

751/251

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 K L P W H F A D L L L E M H S P A A P E  
 N C P G T L Q T C C L K C T A Q Q P L S

781/261

GCT GCT GCC TGC CAC GTC ACG [SEQ ID NO: 3]  
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 L L P A T S [SEQ ID NO: 5]  
 C C L P R H [SEQ ID NO: 6]

T00240" 928TF660

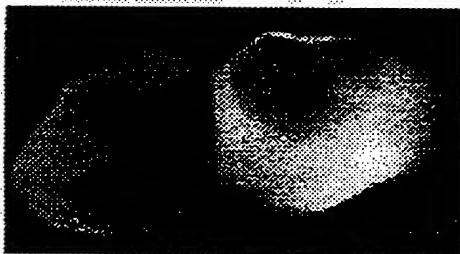
The PDZ domain (but not the C terminal SxV motif)  
is required for plasma membrane localization of  
GRF4

#### GRF4 Localization

WT



-PDZ



-SaV



Figure 20

### Figure 21

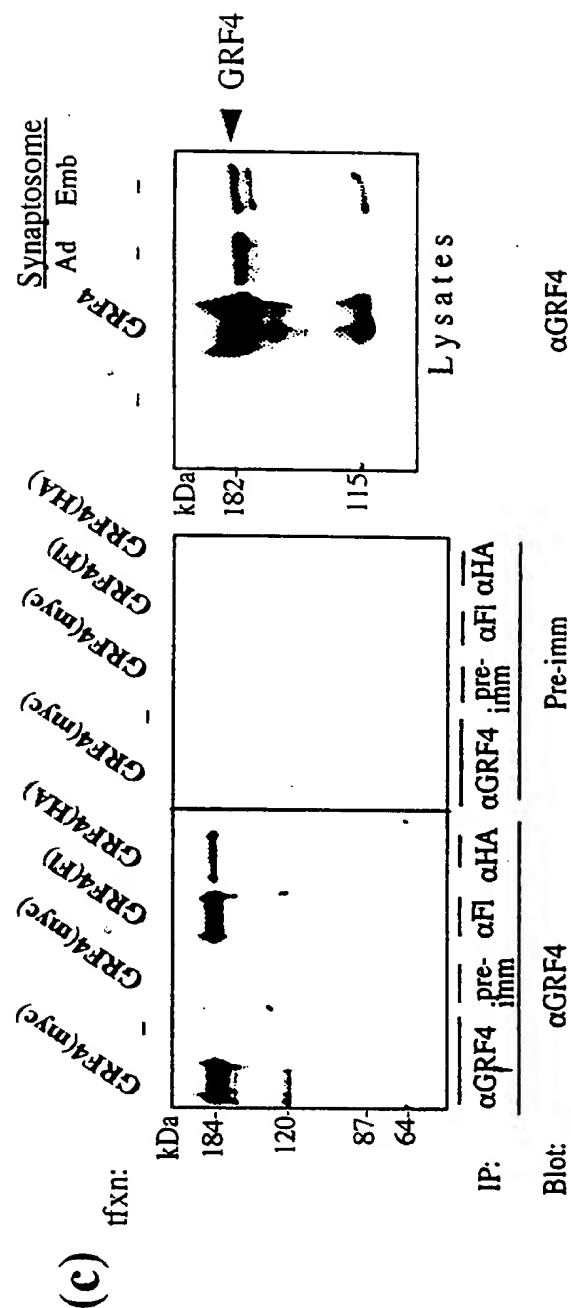
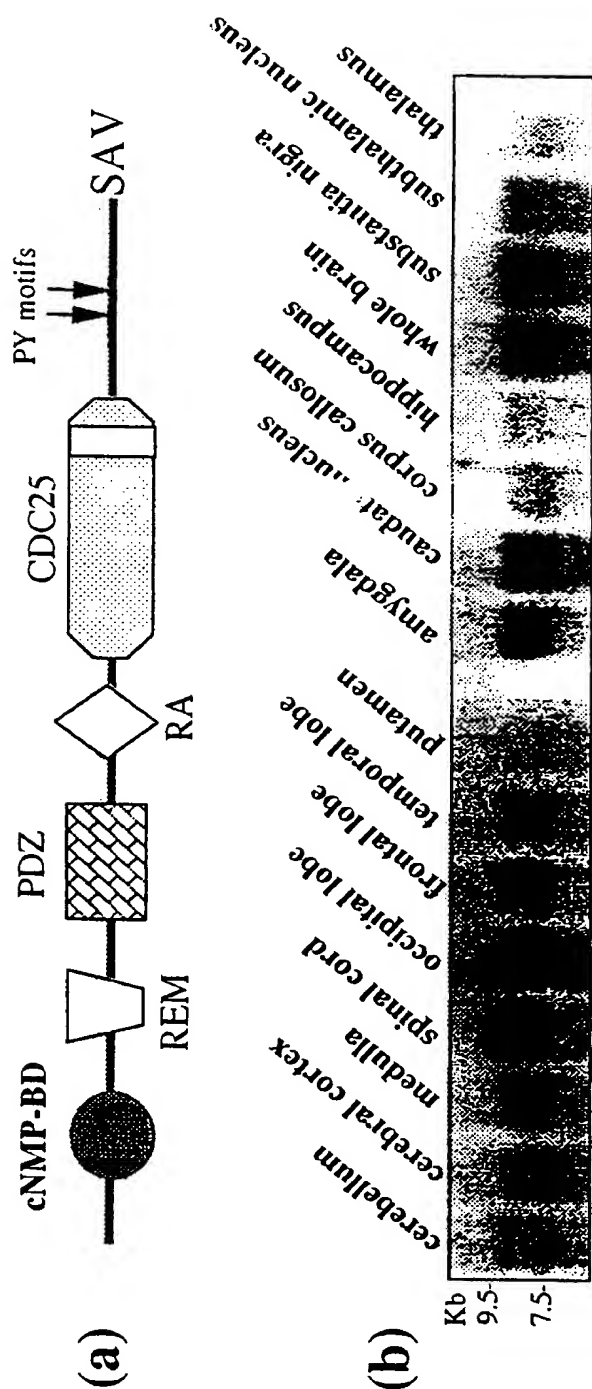
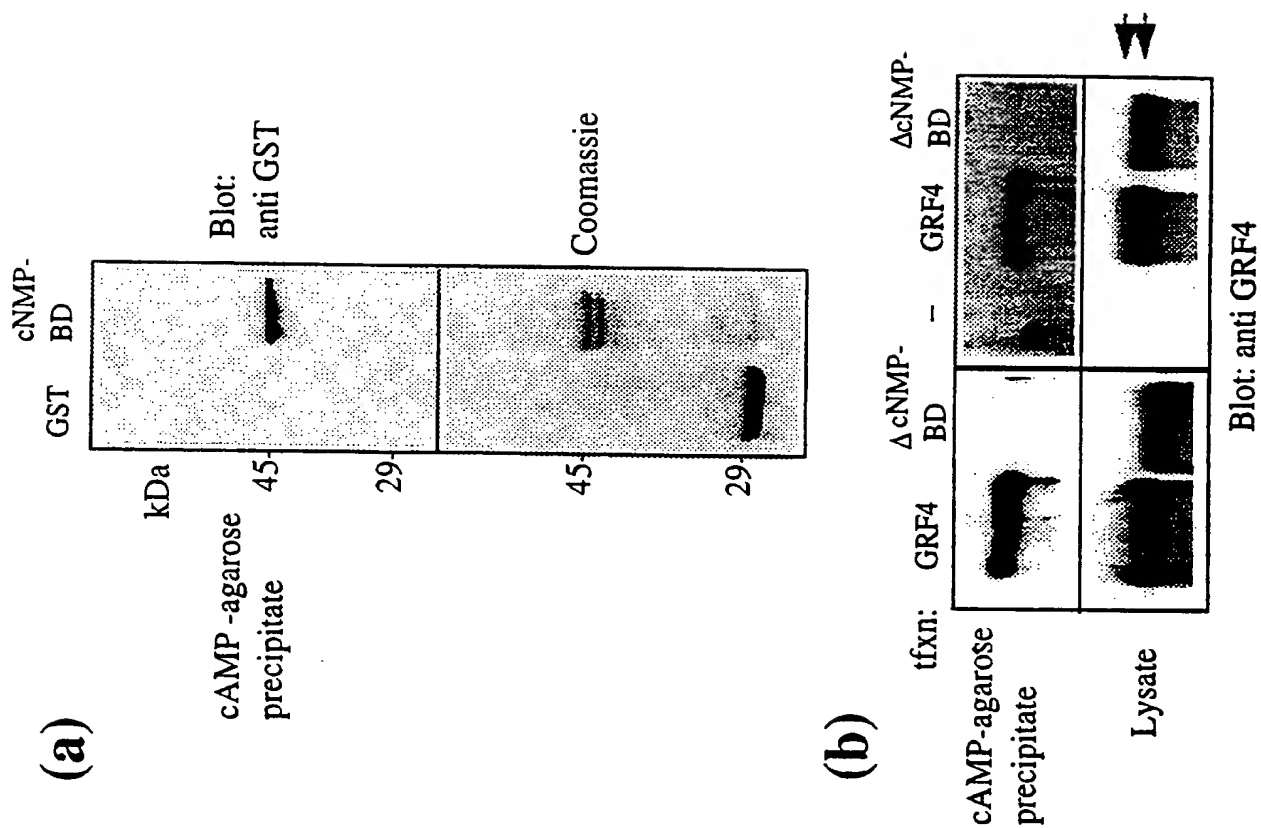


Figure 22





**Figure 23**

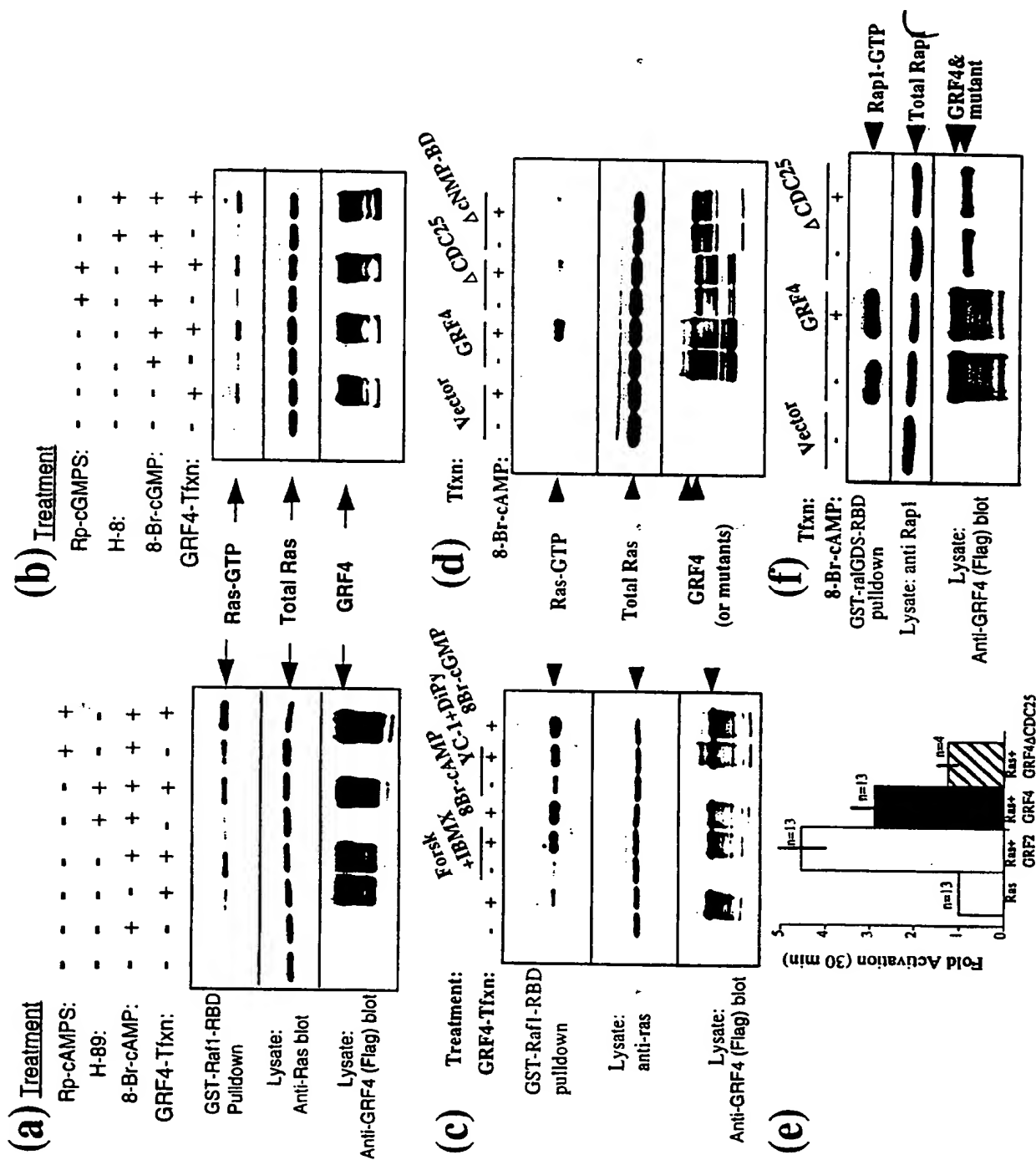


FIG. 24

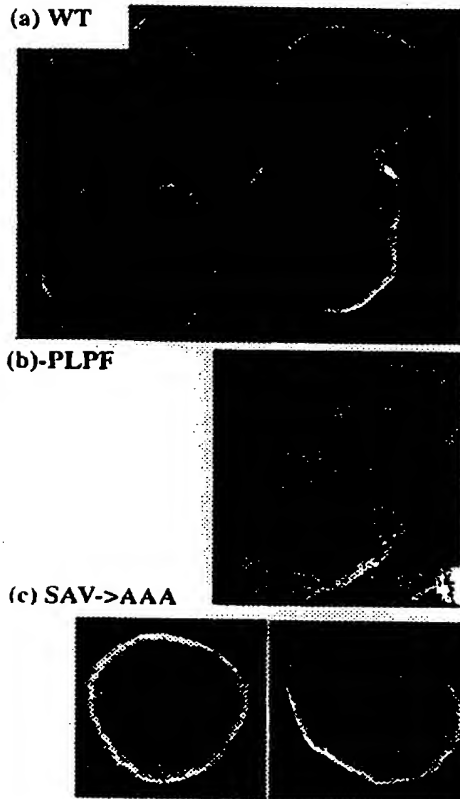


Figure 24